REMARKS

Introductory Comments

Claims 45-48 and 63-65 were examined in the Office Action under reply and stand rejected under 35 U.S.C. §112, first and second paragraphs. These rejections are believed to be overcome for reasons discussed below.

Applicants note with appreciation the withdrawal of the previous rejection under 35 U.S.C. §102(e), as well as the withdrawal of the obviousness-type double patenting rejection.

Applicants again request that withdrawn process claims that depend from or otherwise include all the limitations of allowable product claims be rejoined in accordance with the provisions of MPEP §821.04.

Overview of the Foregoing Amendments

Claim 45 has been amended to recite that the NS3 polypeptide is a "full-length NS3 with amino acids 1027 to 1657 of the HCV polyprotein, numbered relative to HCV-1." Support for this amendment can be found throughout the specification at, for example, page 16, lines 12-21. The amendments are made solely to expedite prosecution, for reasons unrelated to patentability, and do not constitute an acknowledgment that the Examiner's position is correct. In view of the foregoing amendments and following remarks, applicants submit that the application is in condition for allowance and that the amendment should be entered.

Applicants respectfully submit that this claim continues to be patentable over U.S. Patent no. 6,986,892. First, as explained below, applicants are indeed entitled to their priority date of October 27, 1999 which predates the priority date of the '892 patent. However, even if the '892 patent was citable art, it does not teach or suggest fusions as claimed. Rather, the '892 patent is directed to fusions that include mutant non-structural polypeptides, wherein the fusions include a mutated NS3 polypeptide, an NS4 polypeptide and an NS5 polypeptide. Specifically, the mutated NS3 polypeptide includes an **N-terminal deletion** and thus has an amino terminus at amino acid 1242 of the HCV polyprotein. See, the examples of the '892 patent and column 37, lines 62-63. Applicants' claimed NS3 found in the fusions, on the other hand, is full-length and has an amino terminus at amino acid 1027, numbered relative to HCV-1. There is no mention in

the '892 patent of preparing fusion proteins as claimed herein, that include a full-length NS3 polypeptide. Accordingly, the present claims also distinguish over the '892 patent.

Priority

The Office continues to deny applicants the benefit of priority of U.S. provisional application serial No. 60/161,713, filed October 27, 1999. The Office previously stated the '713 application does not include the disclosure of HCV core antigen in any of the immunogenic compositions. However, applicants respectfully disagree.

In particular, as explained in the '713 application, at pages 4-5, bridging paragraph (emphasis added):

> The genomes of HCV strains contain a single open reading frame of approximately 9,000 to 12,000 nucleotides, which is transcribed into a polyprotein. An HCV polyprotein is cleaved to produce at least ten distinct products, in the order of NH2- **Core**-E1-E2-p7-NS2-NS3-NS4a-NS4b-NS5a-NS5b-COOH. Fusion proteins of the invention (NS3NS4NS5a fusion proteins) **comprise** HCV NS3, NS4 (NS4a and NS4b), and NS5a polypeptides (NS3NS4NS5a fusion proteins) or **comprise** HCV NS3, NS4 (NS4a and NS4b), NS5a, and NS5b polypeptides (NS3NS4NS5aNS5b fusion proteins).

The '713 application further explains at page 8, lines 15-23 (emphasis added):

> Polynucleotides contain **less than an entire HCV genome** and can be RNA or single- or double-stranded DNA. Preferably, the polynucleotides are isolated free of other components, such as proteins and lipids. NS3NS4NS5a polynucleotides encode the NS3NS4NS5a fusion proteins described above, and thus **comprise** coding sequences for NS3, NS4, and NS5a polypeptides. NS3NS4NS5aNS5b polynucleotides encode the NS3NS4NS5aNS5b fusion proteins described above, and thus **comprise** coding sequences for NS3, NS4, NS5a, and NS5b polypeptides. Polynucleotides of the invention **can also comprise other nucleotide sequences**, such as sequences coding for linkers, signal sequences, or ligands useful in protein purification such as glutathione-S-transferase and staphylococcal protein A.

When these passages are read together, one of skill in the art would surely understand that fusions including other proteins, such as fusions including additional regions from HCV, were indeed contemplated.

In particular, the first passage above explains that the core region is one of the products cleaved from the polyprotein, along with the NS3, NS4 and NS5 regions.

Moreover, both the first and second passages above make clear that the fusions "comprise" NS3, NS4 and NS5 proteins. Because the term "comprise" is open-ended, the '713 application expressly contemplates that other proteins will be present. Further, the second passage quoted above explicitly states that the polynucleotides contain **less than an entire HCV genome.** Implicit in this statement is that the polynucleotides can include other regions from the HCV genome, so long as the entire genome is not present. This statement, coupled with the explanation that the core region is part of the polyprotein encoded by the genome, makes clear that the inventors contemplated the presence of the core region in the fusions. Finally, the last sentence of the second passage quoted above states polynucleotides of the invention **can also comprise other nucleotide sequences**. When these passages of the application are read in concert, it is clear that a fusion including core in addition to NS3, NS4 and NS5, was indeed intended.

Accordingly, the present claims are entitled to the priority date of the '713 application.

35 U.S.C. §112

Claim 45 was rejected under 35 U.S.C. §112, second paragraph based on the use of the term "native." Applicants submit that the term native is indeed clear and that one of skill in the art would understand this term in the context of HCV. Nevertheless, this term has been eliminated from the claims. Withdrawal of this basis for rejection is therefore respectfully requested.

Claims 45-48 and 63-65 were rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. The Office asserts claim 45 "introduces a new matter that is not supported by the specification as it was originally filed." Office Action, page 4. Applicants respectfully disagree. The Examiner's attention is directed to the definition of an HCV polypeptide found at page 5, lines 15-24 and in particular, lines 22-24 (emphasis added): "Thus, for example, the term 'NS4' polypeptide refers to **native** NS4 from any of the various HCV strains, as well as NS4 analogs, muteins and immunogenic fragments, as defined further below." Although this sentence only refers to NS4, when read in context of the entire paragraph, it is clear that all of the HCV proteins from the polyprotein are included in the definition. Accordingly, adequate basis for the term "native" is indeed present. Nevertheless, this

terminology no longer appears in the claims and this basis for rejection no longer applies.

CONCLUSION

In light of the above remarks, applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at 650-493-3400.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

Please direct all further written communications regarding this application to:

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Respectfully submitted,

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